Adalimumab drug optimisation in rheumatoid arthritis using therapeutic drug monitoring (ADDORA): multi-centre open label randomised controlled trail

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26185

Source
Nationaal Trial Register

Brief title
ADDORA

Health condition

Rheumatoid arthritis

Sponsors and support

Primary sponsor: Reade Rheumatology Research Institute
Source(s) of monetary or material Support: ZonMw: The Netherlands Organisation for Health Research and Development

Intervention

Outcome measures

Primary outcome

The main objective is to evaluate whether adalimumab dose reduction using adalimumab serum concentration will minimize medical costs, compared to disease activity guided dose reduction in rheumatoid arthritis patients

Secondary outcome

The secondary objectives are to investigate the percentage of patients reaching minimal disease activity (DAS28-CRP<2.9) in both study arms; to study the difference in cumulative incidence of flares between the study arms; to evaluate the algorithm used to prolong the dosing interval based on adalimumab concentration; to study the difference in cumulative incidence of flares between both arm after discontinuation of treatment after 52 weeks and 80 weeks

Study description

Background summary

Since the introduction of biologics in rheumatology, as well as treat-to-target (measuring disease activity and adapting treatment accordingly) the prognosis of patients has improved substantially. Obviously, patient burden due to self-injection or infusion, the risk of adverse events and costs demand responsible use of these agents. Multiple studies have shown that a large proportion of patients with rheumatoid arthritis with stable low disease activity can taper their dose or stop without relapse of disease activity. This can be done by using disease activity guided tapering. Drawbacks, however, include increased risk for short lived flares, the effort of slowly and carefully tapering, and somewhat more risk of radiographic damage due to higher mean disease activity.As most biologics are characterized by wide variation in pharmacokinetics between patients, therapeutic drug monitoring (TDM), i.e. dose based on serum trough concentration, might be an attractive approach to lower the dose quickly while remaining clinical efficacy. Although some data suggest that the minimal effective concentration varies between patients, we demonstrated in an earlier study that serum adalimumab concentration of 5 mg/L is enough for initial response to adalimumab. In the first phase of treatment, drug concentration must be high enough to control immunogenicity. To control disease activity after 28 weeks, lower concentrations than 5 mg/L are probably sufficient. Since around 70% of the patients have an adalimumab concentration above 5 mg/l, we assume that dose reduction to achieve these lower targets (for example direct doubling of interval in patients with levels > 10 mg/L) will result in the lowest effective drug dose. Our study group illustrated in 2018 that dose reduction by extending the dosing interval with 50% is non inferior to continuation of standard dose in patients with adalimumab levels > 8mg/L. In other words, measuring drug concentrations can help clinicians to select overexposed patients to reduce the dose of adalimumab without adversely affecting clinical efficiency. We posit that therapeutic drug monitoring can attribute to a more efficient dose reduction strategy. Since steady state drug concentrations are achieved within 16 weeks of treatment, we expect that the dose can be reduced from this point. This is earlier in treatment compared to the strategy using disease activity alone,

namely after 6 months of treatment. Conceptually, such a test can improve disease activity guided dose reduction in two ways: 1) flaring caused by empirical tapering (i.e. through trial and error) below the minimal effective concentration would be avoided, and 2) patients can be directly given their minimum effective dose instead of empirical tapering, thereby saving time and drugs. Our aim is to investigate whether the use of drug levels can attribute to a more efficient dose reduction strategy of adalimumab in patients with RA. In this study we will compare costs and clinical efficiency of two dose reduction strategies: a strategy using drug concentration versus a strategy using disease activity scores. We expect that direct medical costs will be lower in the 'drug concentration guided' strategy because: 1) overexposed patient can reduce the dose more timely and, 2) adalimumab dose can be further reduced after 6 months of treatment since we posit that adalimumab concentration of 2 mg/L is sufficient to control disease.

Study objective

Adalimumab dose reduction based on serum drug concentration will not affect clinical efficacy of adalimumab, while it will minimize medical costs.

Study design

0,4,16,28,40,52,80 weeks

Intervention

Rheumatoid arthritis patients treated with adalimumab will be randomly assigned to a dose reduction strategy using disease activity scores or to a dose reduction strategy using serum drug concentrations

Contacts

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Eligibility criteria

Inclusion criteria

Rheumatoid arthritis patient, according to ACR 1987 or ACR/EULAR 2010 criteria;
Starting adalimumab as the first biological therapy
Who has agreed to participate (written informed consent);
Age 18 years or older.

Exclusion criteria

Scheduled surgery during the follow-up of the study or other pre-planned reasons for treatment discontinuation;
Life expectancy shorter than follow-up period of the study;
Other disease that might flare if adalimumab is tapered like psoriasis, inflammatory bowel disease.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-12-2019
Enrollment:	267
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Plan description
To avoid duplication of research, the gathered data will be shared once all desirable data analysis have been performed and the results are published.

Ethics review

Positive opinion

Date:	03-12-2019
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8208
Other	METC VUmc : METC 2019.190 CCMO NL68946.029.19 EudraCT 2019-001554-25

Study results

Summary results
N/A